

Women and Ischemia Syndrome Evaluation (WISE) Diagnosis and Pathophysiology of Ischemic Heart Disease Workshop

October 2-4, 2002

Session 5

1. Topic and Author

Prognostic value of ischemia testing in the Women's Ischemia Syndrome Evaluation (WISE)

Sheryl F. Kelsey PhD for the WISE investigators.

2. Where we stand in 2002. Overview/rationale for inclusion of topic.

The Women's Ischemia Syndrome Evaluation (WISE) Study is an NHLBI-sponsored multicenter study designed to improve diagnostic testing and pathophysiological understanding of coronary artery disease (CAD) in women. Nine hundred thirty eight women undergoing clinically indicated coronary angiography for chest pain or suspected myocardial ischemia were enrolled between 1996 and 2000. Baseline evaluation included physical exam, coronary angiography, blood cholesterol and reproductive hormone determinations. Site specific testing included coronary flow reserve (CFR) SPECT, stress echo, P31 NMR stress testing, brachial artery endothelial function and quantitative MRI perfusion.

WISE defined "classic ischemia" per non Invasive testing as a positive test on any of the following: SPECT Imaging (Radionuclide Perfusion), Dobutamine Stress Echocardiography, Exercise Stress ECG or Pharmacological ECG.

The 584 WISE women who had at least one non-invasive test were divided into three categories: 1) those with significant coronary artery disease according to core laboratory read angiography; 2) those without CAD, but with classic ischemia and; 3) those with neither CAD nor classic ischemia. Over an average follow-up of 32 months, those with CAD, as expected, had the worse prognosis with regard to mortality, myocardial infarction (MI), stroke, coronary heart failure (CHF) other vascular events and hospitalization for angina. What was not expected, however, was the women diagnosed with classic ischemia, but no CAD, had a better prognosis than those with neither CAD nor classic ischemia.

In women with symptoms but without CAD, why does classic ischemia have a better prognosis than no classic ischemia? We offer several speculations: there are more non-specific other medical problems among those without ischemia or CAD; psychological uncertainty; selection bias as to who can undergo testing (particularly exercise stress testing), medication use and, of most importance, it may well be that the classic ischemia definition is not specific for women.

WISE also employed novel testing to measure dysfunction, possibly ischemia, including brachial flow-mediated dilation, quantitative MRI perfusion, CFR, and ³¹P NMR stress testing. To date, P31 is the best predictor of outcome events. An abnormal P31, but no CAD, had nearly a poor prognosis as CAD. The majority of events were re-hospitalization for angina so that P-31 may be identifying women with persistent symptoms.

3. Current challenges and the most important issues for future research

Although all WISE women underwent angiography, a limitation of the design of WISE was that few women had more than one test to measure ischemia or microvascular dysfunction. Prognostic data for women who have multiple tests would be important so we can judge the relative value of various tests. Development of

an algorithm for which tests should be done to evaluate women presenting with chest pain is needed. There is need to continue to try to unravel the mystery of unexplained chest pain symptoms in women. Do these women have ischemia that we haven't been able to detect?

4. Current challenges in the areas of communicating messages to health care community, patients and the public

Women who present with chest pain and suspected ischemia and are determined not to have CAD nevertheless experience considerable morbidity and resource utilization. These symptoms need to be taken seriously, appropriately assessed and therapy, more than reassurance offered. Small randomized trials indicate that ACE inhibitors, L-arginine, estrogen, and tricyclic therapies may be efficacious for these women.

5. Translating new findings to improved diagnosis and treatment/saving lives.

We need to stress the importance of further evaluation after CAD has been ruled out. An important goal is to develop cost effective testing algorithms for symptomatic women to diagnoses ischemia in the absence of CAD.

6. References.